



## EDITORIAL COMMENT

# Renal failure in decompensated heart failure patients: Double trouble



## Insuficiência renal em doentes com insuficiência cardíaca descompensada: um problema duplo

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The association between cardiac and renal disease has been an area of growing interest in recent years. The interactions between these organs play an important role in control of blood pressure, renal sodium and water excretion, arterial perfusion and tissue oxygenation, and, most importantly, extracellular fluid balance, including intravascular volume. It is therefore not surprising that, when one organ becomes dysfunctional, the other may be affected as well.

Heart failure (HF) interacts with renal disease via several pathophysiological pathways in both acute and chronic settings. The expression 'cardiorenal syndrome' has often been used in the last decade to define this interdependency of the kidneys and the heart, and as an umbrella term for worse outcome when the two organs fail simultaneously. A recent review of the pathophysiological pathways of this syndrome was recently published by Schefold et al.<sup>1</sup>

Although the concept of the cardiorenal syndrome is helpful when describing these heart-kidney interactions, it should be emphasized that the current definition of cardiorenal syndrome includes all forms of two-way connections and is not specific to HF.

That being said, it is widely documented that renal dysfunction occurs frequently in all phenotypes of HF, and when present, is associated with higher mortality and morbidity.

Over 50 studies have been published describing the association between renal dysfunction and mortality in HF.<sup>2</sup> The majority of these studies were observational, since most randomized clinical trials on HF exclude patients with moderate to severe chronic kidney disease (CKD). However, two landmark retrospective analyses of randomized controlled trials showed that reductions in estimated glomerular filtration rate (eGFR) were associated with higher mortality.<sup>3,4</sup>

### Worsening renal function

Several meta-analyses have also demonstrated that worsening renal function (WRF) is associated with increased mortality in both inpatients and outpatients, with larger increases in serum creatinine predicting worse outcomes.<sup>2,5,6</sup> It has been observed that even a small increase in serum creatinine during hospitalization, as low as 0.2 mg/dl, is associated with poor outcomes.<sup>7</sup>

However, at least in acute decompensated heart failure (ADHF), some increase in serum creatinine may be acceptable, as long as the patient's overall clinical status does not deteriorate.<sup>8</sup> Patients with WRF and some degree of hemoconcentration, decongestion, or reduction in blood

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pressure resulting from acute HF treatment, especially with diuretics, have a much better outcome than those who have WRF that appears to be unprovoked.<sup>9–11</sup> In other words, as suggested by Damman et al., if a patient's clinical status improves or remains the same and their serum creatinine increases, this 'pseudo-WRF' may not necessarily mean a poor prognosis.<sup>8</sup>

On the other hand, Gottlieb et al. found that 47% of patients admitted for ADHF had WRF during the first three days of hospitalization, when they were still hypervolemic.<sup>7</sup> This finding challenges the common conception that worsening renal function in ADHF is due to decreased intravascular volume and/or low cardiac output. Clearly overdiuresis and lowering filling pressure can potentially worsen renal function, but this is not the case in almost half of ADHF admissions.

### Renal function on admission for decompensated heart failure

According to Damman et al., around 4.5% of the general population have eGFR <60 ml/min/1.73 m<sup>2</sup>, normally classified as chronic kidney disease (CKD), while over 50% of patients with acute and chronic HF (both preserved and reduced ejection fraction) have a similar reduction in eGFR.<sup>2</sup>

It is therefore not surprising that a large percentage of patients admitted to hospital with ADHF present with some degree of renal dysfunction. The exact proportion varies according to the definition of renal failure and the methods used to determine renal function.

Determination of the prognostic significance of low eGFR in ADHF patients on admission in the real world could provide valuable information, considering the increased risk of these patients and the potential implications for therapeutic choices.

It is well known that patients with renal dysfunction are less likely to be treated with drugs like angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, spironolactone or sacubitril, that can improve HF prognosis, for fear of causing renal dysfunction and electrolyte imbalance.

The study by Formiga et al. published in this issue of the *Journal*<sup>12</sup> sheds more light on this important subject. This observational study included nearly 1000 patients with a first episode of ADHF (52.3% of whom had eGFR <60 ml/min), and assessed the one-year prognostic significance of renal dysfunction on admission.

The study's strengths and limitations are well described in the discussion of the paper and should be taken into account when analyzing its results and conclusions.

In our view, the major limitation of this paper (which is also acknowledged by the authors) lies in the fact that data on changes in patients' eGFR during and after hospitalization were not collected, and so the role of worsening or improving renal function (beyond the spot admission data) in the prognosis of the study population could not be assessed.

Despite this limitation, the study's results support the authors' conclusions that assessment of renal failure by the

determination of admission eGFR has significant short- and medium-term prognostic value.

In conclusion, careful reading of Formiga et al. is recommended and physicians should understand that patients with combined renal and heart failure have problems that are more than the sum of these diseases alone.

The management of these patients cannot be based on treating both diseases as separate entities. Many pathophysiological and therapeutic factors must be taken into account and a balance sought between hemodynamic and renal factors for each individual. Getting this balance right can favorably modify the patient's prognosis.

### Conflicts of interest

Daniel Ferreira has received honoraria (advisory board member and/or invited speaker) from Astellas, Astra-Zeneca, Bayer, BMS/Pfizer, Boehringer-Ingelheim, Novartis, and Sanofi-Aventis.

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